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09/926817

INTERNATIONAL APPLICATION NO.
PCT/JP00/06493

INTERNATIONAL FILING DATE
SEPTEMBER 22, 2000

PRIORITY DATE CLAIMED
APRIL 21, 2000

TITLE OF INVENTION

MULTI-LAYERED TUBE AND MEDICAL DEVICE COMPRISING THE MULTI-LAYERED TUBE

APPLICANT(S) FOR DO/EO/US
Yukihiko FUJIEDA, et al.

Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:

1. ☒ This is a **FIRST** submission of items concerning a filing under 35 U.S.C. 371.
2. ☐ This is a **SECOND** or **SUBSEQUENT** submission of items concerning a filing under 35 U.S.C. 371.
3. ☒ This is an express request to begin national examination procedures (35 U.S.C. 371(f)). The submission must include items (5), (6), (9) and (24) indicated below.
4. ☐ The US has been elected by the expiration of 19 months from the priority date (Article 31).
5. ☒ A copy of the International Application as filed (35 U.S.C. 371 (c) (2))
 - a. ☐ is attached hereto (required only if not communicated by the International Bureau).
 - b. ☒ has been communicated by the International Bureau.
 - c. ☐ is not required, as the application was filed in the United States Receiving Office (RO/US).
6. ☒ An English language translation of the International Application as filed (35 U.S.C. 371(c)(2)).
 - a. ☒ is attached hereto.
 - b. ☐ has been previously submitted under 35 U.S.C. 154(d)(4).
7. ☒ Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371 (c)(3))
 - a. ☐ are attached hereto (required only if not communicated by the International Bureau).
 - b. ☐ have been communicated by the International Bureau.
 - c. ☐ have not been made; however, the time limit for making such amendments has NOT expired.
 - d. ☒ have not been made and will not be made.
8. ☐ An English language translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).
9. ☒ An oath or declaration of the inventor(s) (35 U.S.C. 371 (c)(4)).
10. ☒ An English language translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371 (c)(5)).
11. ☐ A copy of the International Preliminary Examination Report (PCT/IPEA/409).
12. ☒ A copy of the International Search Report (PCT/ISA/210).

Items 13 to 20 below concern document(s) or information included:

13. ☒ An Information Disclosure Statement under 37 CFR 1.97 and 1.98.
14. ☐ An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.
15. ☒ A **FIRST** preliminary amendment.
16. ☐ A **SECOND** or **SUBSEQUENT** preliminary amendment.
17. ☐ A substitute specification.
18. ☐ A change of power of attorney and/or address letter.
19. ☐ A computer-readable form of the sequence listing in accordance with PCT Rule 13ter.2 and 35 U.S.C. 1.821 - 1.825.
20. ☐ A second copy of the published international application under 35 U.S.C. 154(d)(4).
21. ☐ A second copy of the English language translation of the international application under 35 U.S.C. 154(d)(4).
22. ☐ Certificate of Mailing by Express Mail
23. ☒ Other items or information:

Drawing (3 Sheets)
Form PTO 1449

PCT/JP00/06493

ATTORNEY'S DOCKET NUMBER
217411US0XPCT

24. The following fees are submitted:

BASIC NATIONAL FEE (37 CFR 1.492 (a) (1) - (5)) :

- ☐ Neither international preliminary examination fee (37 CFR 1.482) nor international search fee (37 CFR 1.445(a)(2)) paid to USPTO and International Search Report not prepared by the EPO or JPO \$1040.00
- ☒ International preliminary examination fee (37 CFR 1.482) not paid to USPTO but International Search Report prepared by the EPO or JPO \$890.00
- ☐ International preliminary examination fee (37 CFR 1.482) not paid to USPTO but international search fee (37 CFR 1.445(a)(2)) paid to USPTO \$740.00
- ☐ International preliminary examination fee (37 CFR 1.482) paid to USPTO but all claims did not satisfy provisions of PCT Article 33(1)-(4) \$710.00
- ☐ International preliminary examination fee (37 CFR 1.482) paid to USPTO and all claims satisfied provisions of PCT Article 33(1)-(4) \$100.00

ENTER APPROPRIATE BASIC FEE AMOUNT =

\$890.00

Surcharge of \$130.00 for furnishing the oath or declaration later than ☐ 20 ☐ 30 months from the earliest claimed priority date (37 CFR 1.492 (e)).

\$0.00

CLAIMS	NUMBER FILED	NUMBER EXTRA	RATE
Total claims	17 - 20 =	0	x \$18.00
Independent claims	1 - 3 =	0	x \$84.00
Multiple Dependent Claims (check if applicable)			<input type="checkbox"/>

\$0.00

\$0.00

\$0.00

TOTAL OF ABOVE CALCULATIONS =

\$890.00

☐ Applicant claims small entity status. See 37 CFR 1.27. The fees indicated above are reduced by 1/2.

\$0.00

SUBTOTAL =

\$890.00

Processing fee of \$130.00 for furnishing the English translation later than ☐ 20 ☐ 30 months from the earliest claimed priority date (37 CFR 1.492 (f)).

\$0.00

TOTAL NATIONAL FEE =

\$890.00

Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31) (check if applicable).

\$0.00

TOTAL FEES ENCLOSED =

\$890.00

Amount to be:	\$
refunded	
charged	\$

- ☒ A check in the amount of \$890.00 to cover the above fees is enclosed.
- b. ☐ Please charge my Deposit Account No. _____ in the amount of _____ to cover the above fees. A duplicate copy of this sheet is enclosed.
- c. ☒ The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 15-0030. A duplicate copy of this sheet is enclosed.
- d. ☐ Fees are to be charged to a credit card. **WARNING:** Information on this form may become public. **Credit card information should not be included on this form.** Provide credit card information and authorization on PTO-2038.

NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b)) must be filed and granted to restore the application to pending status.

SEND ALL CORRESPONDENCE TO:

Surinder Sachar
Registration No. 34,423



22850

SIGNATURE

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NAME

24,618

REGISTRATION NUMBER

DATE

Dec. 21 2001

09/926817

JC07 Rec'd PCT/PTO 21 DEC 2001

217411US-0XPCT

IN THE UNITED STATES PATENT & TRADEMARK OFFICE

IN RE APPLICATION OF :
YUKIHIRO FUJIEDA ET AL : ATTN: APPLICATION DIVISION
SERIAL NO: NEW U.S. PCT APPLN :
(Based on PCT/JP00/06493)
FILED: HEREWITH :
FOR: MULTI-LAYERED TUBE AND :
MEDICAL DEVICE COMPRISING
MULTI-LAYERED TUBE

PRELIMINARY AMENDMENT

ASSISTANT COMMISSIONER FOR PATENTS
WASHINGTON, D.C. 20231

SIR:

Prior to examination on the merits, please amend the above-identified application as follows.

IN THE CLAIMS

Please amend the claims as shown on the marked-up copy following this amendment to read as follows.

4. (Amended) The multi-layered tube of claim 1, wherein said layer (II) is a layer (II-1) formed of a resin composition containing 45 to 70 mass% of the polypropylene resin (a) and 55 to 30 mass% of the copolymer (b).

5. (Amended) The multi-layered tube of claim 1, wherein said layer (II) is a layer (II-2) formed of a resin composition containing 70 to 100 mass% of the polypropylene resin (a) and 30 to 0 mass% of the copolymer (b).

8. (Amended) The multi-layered tube of claim 6, wherein said layer (II) is a layer (II-1) formed of a resin composition containing 45 to 70 mass% of the polypropylene resin (a) and 55 to 30 mass% of the copolymer (b).

9. (Amended) The multi-layered tube of claim 6, wherein, in the said three-layered tube, said outer layer is a layer (II-1) formed of a resin composition containing 45 to 70 mass% of the polypropylene resin (a) and 55 to 30 mass% of the copolymer (b),

said intermediate layer is the layer (I) formed of a resin composition containing 5 to 40 mass% of the polypropylene resin (a) and 95 to 60 mass% of the copolymer (b), and

said inner layer is a layer (II-2) formed of a resin composition containing 70 to 100 mass% of the polypropylene resin (a) and 30 to 0 mass% of the copolymer (b).

10. (Amended) The multi-layered tube of claim 1, wherein said hydrogenated block copolymer (b1) has a vinyl aromatic compound component content of 10 to 40 mass%, the isoprene polymer block (B) has a 1,2-bond and 2,4-bond content of 10 to 75 mol%, and at least 70% of carbon-carbon double bonds of the block copolymer (b1) are hydrogenated.

11. (Amended) The multi-layered tube of claim 1, wherein said hydrogenated block copolymer (b2) has a vinyl aromatic compound component content of 10 to 40 mass%, the polymer block (C) has an isoprene component/butadiene component weight ratio of 5/95 to 95/5 and a 1,2-bond and 3,4-bond content of 20 to 85 mol%, and at least 70% of carbon-carbon double bonds of the block copolymer (b2) are hydrogenated.

12. (Amended) The multi-layered tube of claim 1, wherein said hydrogenated block copolymer (b3) has a vinyl aromatic compound component content of 10 to 40 mass%, the

butadiene polymer block (D) has a 1,2-bond content of at least 30 mol%, and at least 70% of carbon-carbon double bonds of the block copolymer (b3) are hydrogenated.

13. (Amended) The multi-layered tube of claim 1, wherein said vinyl aromatic compound is styrene.

14. (Amended) The multi-layered tube of claim 1, wherein said tube is a multi-layered tube for medical use.

15. (Amended) The multi-layered tube of claim 14, wherein said tube is for forming a circuit for extracorporeal circulation.

16. (Amended) The multi-layered tube of claim 1, wherein the polypropylene resin (a) forming said layer (I) has a bending flexural modulus of 200 to 400 MPa and the polypropylene resin (a) forming said layer (II) has a flexural modulus of 500 to 900 MPa.

17. (Amended) A medical device comprising the multi-layered tube recited in claim 1 and other member to which said multi-layered tube is connected.

REMARKS

Claims 1-17 are active in the present application. Claims 4-5 and 8-17 have been amended to remove multiple dependencies. No new matter is added. An action on the merits and allowance of claims is solicited.

Respectfully submitted,

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Marked-Up Copy

Serial No:

Amendment Filed on:

12-21-01

IN THE CLAIMS

Please amend the claims to read as follows:

--4. (Amended) The multi-layered tube of [any one of claims 1 to 3] claim 1, wherein said layer (II) is a layer (II-1) formed of a resin composition containing 45 to 70 mass% of the polypropylene resin (a) and 55 to 30 mass% of the copolymer (b).

5. (Amended) The multi-layered tube of [any one of claims 1 to 3] claim 1, wherein said layer (II) is a layer (II-2) formed of a resin composition containing 70 to 100 mass% of the polypropylene resin (a) and 30 to 0 mass% of the copolymer (b).

8. (Amended) The multi-layered tube of claim 6 [or 7], wherein said layer (II) is a layer (II-1) formed of a resin composition containing 45 to 70 mass% of the polypropylene resin (a) and 55 to 30 mass% of the copolymer (b).

9. (Amended) The multi-layered tube of [any one of claims 6 to 8] claim 6, wherein, in the said three-layered tube, said outer layer is a layer (II-1) formed of a resin composition containing 45 to 70 mass% of the polypropylene resin (a) and 55 to 30 mass% of the copolymer (b),

said intermediate layer is the layer (I) formed of a resin composition containing 5 to 40 mass% of the polypropylene resin (a) and 95 to 60 mass% of the copolymer (b), and

said inner layer is a layer (II-2) formed of a resin composition containing 70 to 100 mass% of the polypropylene resin (a) and 30 to 0 mass% of the copolymer (b).

10. (Amended) The multi-layered tube of [any one of claims 1 to 9] claim 1, wherein said hydrogenated block copolymer (b1) has a vinyl aromatic compound component content of 10 to 40 mass%, the isoprene polymer block (B) has a 1,2-bond and 2,4-bond content of 10 to 75 mol%, and at least 70% of carbon-carbon double bonds of the block copolymer (b1) are hydrogenated.

11. (Amended) The multi-layered tube of [any one of claims 1 to 9] claim 1, wherein said hydrogenated block copolymer (b2) has a vinyl aromatic compound component content of 10 to 40 mass%, the polymer block (C) has an isoprene component/butadiene component weight ratio of 5/95 to 95/5 and a 1,2-bond and 3,4-bond content of 20 to 85 mol%, and at least 70% of carbon-carbon double bonds of the block copolymer (b2) are hydrogenated.

12. (Amended) The multi-layered tube of [any one of claims 1 to 9] claim 1, wherein said hydrogenated block copolymer (b3) has a vinyl aromatic compound component content of 10 to 40 mass%, the butadiene polymer block (D) has a 1,2-bond content of at least 30 mol%, and at least 70% of carbon-carbon double bonds of the block copolymer (b3) are hydrogenated.

13. (Amended) The multi-layered tube of [any one of claims 1 to 12] claim 1, wherein said vinyl aromatic compound is styrene.

14. (Amended) The multi-layered tube of [any one of claims 1 to 13] claim 1, wherein said tube is a multi-layered tube for medical use.

15. (Amended) The multi-layered tube of [claims] claim 14, wherein said tube is for forming a circuit for extracorporeal circulation.

16. (Amended) The multi-layered tube of [any one of claims 1 to 15] claim 1, wherein the polypropylene resin (a) forming said layer (I) has a bending flexural modulus of

200 to 400 MPa and the polypropylene resin (a) forming said layer (II) has a flexural modulus of 500 to 900 MPa.

17. (Amended) A medical device comprising the multi-layered tube recited in [any one of claims 1 to 16] claim 1 and other member to which said multi-layered tube is connected.--

3/PATS

DESCRIPTION

Multi-layered Tube and
Medical Device Comprising the Multi-layered Tube

Technical Field

The present invention relates to a multi-layered tube and a medical device comprising the multi-layered tube. More specifically, the present invention relates to a multi-layered tube for medical use which is excellent in flexibility, transparency, anti-kinking properties and restoration capability after occlusion, which also has durability against high-pressure steam sterilization, and which is excellent in connectability to other tube having a different diameter, a connector, a joint, and the like.

The multi-layered tube of the present invention is suitable for use as a component for medical devices such as a blood circuit line, a blood bag, a medicinal fluid bag, a blood transfusion/infusion set, a catheter, and the like.

Technical Background

Polyvinyl chloride has been and is widely used not only in the fields of industries and household articles but also in the fields of medical treatment and welfare. Particularly, most of disposable medical devices are produced from polyvinyl chloride. Since, however, soft polyvinyl chloride contains a relatively large amount of plasticizers such as dioctyl phthalate (DOP), etc., the problem of elution of the plasticizer into blood or a medicinal solution is pointed out from the viewpoint of safety of medical devices.

On the other hand, from the viewpoint of infection prevention, steps are taken forward to dispose medical devices, and it is required by the law to dispose of used medical devices by incineration. It is said that polyvinyl chloride generates almost no toxic chlorine-containing

substances such as dioxin since it is converted finally to carbon dioxide, water and hydrogen chloride when combusted at a temperature of approximately 850 to 900°C with feeding sufficient oxygen. In reality, however, the problem of environmental pollution with dioxin or other toxic chlorine-containing substance frequently takes place for reasons that there are not sufficient incinerators that can withstand said high temperatures, that there are small-sized incinerators of which the incineration capacity is insufficient and that there are few plants for dioxin disposal.

Studies are recently being made for changing the material in the fields of medical devices, industries and household devices from the soft vinyl chloride to other materials.

As a polyvinyl-chloride-free material for medical tubes, studies are made on polyethylene (PE), polypropylene (PP), an ethylene-vinyl acetate copolymer (EVAC), polyethyl methacrylate (PEMA), a styrene-butadiene block copolymer, a hydrogenation product of a styrene-isoprene copolymer (styrene-based thermoplastic elastomer), and the like.

For example, as a resin composition that gives a molded article excellent in flexibility and suitable for medical use, JP-A-4-158868 (Literature 1), JP-A-4-159344 (Literature 2) and JP-A-8-131537 (Literature 3) propose a resin composition (styrene-based thermoplastic elastomer) containing an olefin resin, a hydrogenation product of a styrene-butadiene block copolymer (styrene-based thermoplastic elastomer) and a hydrogenation product of a styrene-isoprene block copolymer.

Further, JP-A-9-103493 (Literature 4) and JP-A-123314 (Literature 5) disclose a multi-layered tube formed of a substrate layer and an adhesive layer in which the adhesive layer is made of a material that is not dimensionally stable at an autoclave sterilization temperature (121°C) or higher and tends to flow under a connection pressure with other tube having a different diameter during autoclave sterilization at

121°C.

(1) In principle, however, a tube made of the above PE, EVAC or PEMA has flexibility but has a problem that the tube, when made of a single material, is liable to undergo kinking (which refers to a phenomenon that the tube bends or is twisted to come into the state where internal surfaces of the tube become stuck or adhered together).

(2) While the above styrene-based thermoplastic elastomer as a single material or a composition containing 60 mass% thereof or more has flexibility, they come to have sticking nature on the surface when sterilized with high-pressure steam (autoclave sterilization), so that they are not suitable for use as a material to form a surface that will contact blood. Further, they have a problem that the internal surface of the tube undergoes self-sticking (self-adhesion) when the tube is clamped with a forceps and the tube shows poor restoration capability when it was released from clamping after occlusion.

(3) Further, a tube made of the above PP as a single material or a composition containing at least 40 mass% thereof is too rigid and not flexible enough to prevent kinking.

The resin composition described in the above Literatures 1 to 3 has characteristic features that it gives a molded article excellent in flexibility and it does not involve the generation of an toxic gas such as dioxin when the molded article is incinerated. However, ① when emphasis is placed on flexibility, a single-layered tube made of the above resin composition has a higher proportion of the styrene-based thermoplastic elastomer, and the tube suffers problems that are not negligible, that is, it has poor heat resistance problem that the cross section of the tube sterilized in an autoclave is deformed or one tube is fused with another or a problem that the tube has poor restoration capability when released from clamping with a forceps after occlusion with it. ② When emphasis is placed on heat

resistance and restoration capability after occlusion, the proportion of the styrene-based thermoplastic elastomer comes to be smaller, and the tube becomes less flexible and is not at all satisfactory as a medical tube. It is therefore
5 desired to improve the tube in these points.

In a multi-layered tube, hot melt bonding or solvent bonding is the most preferred in view of reliable connection. In the multi-layered tube described in Literature 4 or 5, the adhesive layer is made of a material that is not
10 dimensionally stable at an autoclave sterilization temperature (121°C) or higher and tends to flow under a connection pressure with other tube having a different diameter during autoclave sterilization at 121°C, and the tube is connected to the other tube by "press fitting"
15 between these tubes. These tubes are therefore intimately connected by adherence, so that one tube easily comes off from the other under small force. Further, since tackiness is caused under heat by the autoclave sterilization, fitted portions may come apart one from the other during the
20 sterilization or at a step prior thereto, and it is considered that such a material is not suitable for producing medical devices.

As performances required for medical tube that can be sterilized with high-pressure steam, preferably, the tube
25 satisfies the following conditions:

That is, (a) the tube is to have proper flexibility without keeping on kinking or bending when bent, (b) the tube is to show no stickiness (tackiness) on the surface and is to be free from any change in form and dimensions when
30 sterilized with high-pressure steam, and (c) the tube permits hot melt bonding or solvent bonding when connected to other tube having a different diameter or an injection-molded article.

As described above, it is an object of the present
35 invention to provide a multi-layered tube which is excellent in transparency, flexibility, anti-kinking properties,

restoration capability after occlusion and heat resistance and which elutes no plasticizer and generates no toxic gas when incinerated, and to provide a medical device comprising said multi-layered tube.

Disclosure of the Invention

The present inventors have made diligent studies from the above viewpoints and as a result have found that the above object can be achieved by providing a multi-layered tube having layers having different compositions comprising a polypropylene resin and at least one copolymer selected from a hydrogenated block copolymer of a polymer block from a vinyl aromatic compound and an isoprene and/or butadiene block and a hydrogenation product of a copolymer from a vinyl aromatic compound and butadiene, and a medical device comprising the above multi-layered tube. The present invention has been accordingly made.

That is, according to the present invention, there are provided the following inventions [1] and [2].

[1] A multi-layered tube composed of at least two layers, wherein at least one layer of said layers is a layer (I) made of a resin composition comprising 5 to 40 mass% of a polypropylene resin (a),

and 95 to 60 mass% of at least one copolymer (b) selected from the group consisting of

a hydrogenated block copolymer (b1) obtained by hydrogenation of a block copolymer formed of a polymer block (A) from a vinyl aromatic compound and an isoprene polymer block (B),

a hydrogenated block copolymer (b2) obtained by hydrogenating a block copolymer formed of a polymer block (A) from a vinyl aromatic compound and a polymer block (C) from isoprene and butadiene,

a hydrogenated block copolymer (b3) obtained by hydrogenating a block copolymer formed of a polymer block (A)

from a vinyl aromatic compound and a butadiene polymer block (D), and

a hydrogenated copolymer (b4) obtained by hydrogenating a copolymer of a vinyl aromatic compound and butadiene, and

at least one layer of the remaining layer or layers is a layer (II) formed of a resin composition comprising 45 to 100 mass% of a polypropylene resin (a) and 55 to 0 mass% of the above copolymer (b), and

further wherein said layer (I) forms one layer of an inner layer and an outer layer and said layer (II) forms the other layer, or said layer (I) forms an intermediate layer and the layer (II) forms the inner layer and the outer layer.

[2] A medical device comprising said multi-layered tube and other member to which said multi-layered tube is connected.

Brief Description of Drawings

Fig. 1 shows cross-sectional views of multi-layered tubes 1 of the present invention. Fig. 2 is a partially enlarged longitudinal sectional view of a medical device comprising the multi-layered tube of the present invention connected to other connection member having a different diameter. Fig. 3 is a partially enlarged longitudinal sectional view of a medical device comprising the multi-layered tube of the present invention connected to other connection member having a different diameter.

In the drawings, 1 indicates a multi-layered tube, 3 indicates an inner layer, 5 indicates an outer layer, 7 indicates an intermediate layer, 50 indicates a connection member, 55 indicates an internal surface of the connection member, 57 indicates an external surface of the connection member, I indicates a layer (I), and II indicates a layer (II).

Preferred Embodiments of the Invention

The present invention will be explained in detail hereinafter.

5 The polypropylene resin (a) for constituting the multi-layered tube of the present invention can be selected from known polypropylene resins, and it may be any one of homo polypropylene, random polypropylene and block polypropylene. The polypropylene resins (a) may be used
10 alone or in combination. Basically, when measured according to ASTM D-1238 at 230°C under a load of 2,160 g, the polypropylene resin (a) preferably has a melt flow rate (MFR) in the range of from 0.1 to 500, more preferably in the range of from 0.1 to 200.

15 As a polypropylene resin for the layer (I), the above polypropylene preferably has a bending flexural modulus of 200 to 400 MPa (crystallinity of 30 to 40 % and a molecular weight of 50,000 to 200,000). As a polypropylene resin for the layer (II), the above polypropylene preferably
20 has a bending flexural modulus of 500 to 900 MPa (crystallinity of at least 50 % and a molecular weight of 100,000 to 500,000).

In principle, the layer (I) is a layer that forms a component constituting a substrate of the multi-layered tube,
25 and the layer (II) is a layer that works as a connection layer when the multi-layered tube is connected to other part to form a medical device.

When the polypropylene resin to be incorporated into the layer (I) has a bending flexural modulus in the above
30 range, the tube can be imparted with flexibility and anti-kinking properties. When the flexural modulus is less than 200 MPa, the tube is too soft and exhibits no nerve (stiffness). When it exceeds 400 MPa, undesirably, the tube is liable to keep on kinking and bending when bent.

35 When the polypropylene resin to be incorporated into the layer (II) has a bending flexural modulus in the above

range, the layer (II) can be imparted with a nerve (stiffness) so that flowing of the layer (II) during sterilization with high-pressure steam can be prevented.

The copolymer (b) used in the present invention is a hydrogenating block copolymer ((b1) - (b3)) obtained by hydrogenating a copolymer formed of a polymer block (A) from a vinyl aromatic compound and a polymer block ((B) - (D)) from an isoprene and/or butadiene, or a hydrogenated copolymer (b4) obtained by hydrogenating a copolymer of a vinyl aromatic compound and butadiene.

In the hydrogenated block copolymers ((b1) - (b3)), the vinyl aromatic compound is preferably styrene, and the hydrogenated block copolymers ((b1) - (b3)) are desirably a hydrogenated product (b1) of a styrene-isoprene-styrene copolymer, a hydrogenated product (b2) of a styrene-isoprene/butadiene-styrene copolymer, a hydrogenated product (b3) of a styrene-butadiene-styrene copolymer, and the like.

The hydrogenated copolymer (b4) is a hydrogenated copolymer obtained by hydrogenating a copolymer of a vinyl aromatic compound and butadiene as described above. Preferably, the vinyl aromatic compound is styrene, and the hydrogenated copolymer (b4) is a hydrogenated styrene-butadiene-rubber. It is particularly desirable to use a type of the hydrogenated copolymer (b4) that is ultra-finely dispersible in polypropylene.

As a vinyl aromatic compound for the copolymer (b), such vinyl aromatic compounds as described later can be used besides the styrene.

In the present invention, the layer (I) is a layer formed of a resin composition containing 5 to 40 mass%, preferably 15 to 35 mass%, more preferably 20 to 30 mass% of the polypropylene resin (a) and 95 to 60 mass%, preferably 85 to 65 mass%, more preferably 80 to 70 mass% of the copolymer (b).

Basically, the multi-layered tube of the present invention has the layer (I) as a substrate layer, so that the

multi-layered tube can be imparted with flexibility and anti-kinking properties. That is, when the content of the copolymer (b) exceeds 95 mass%, the tube is too soft and has no nerve, and when the tube is closed with a medical tube

5 forceps for 15 hours and then released from the forceps, the tube does not easily gain a through passage inside the tube within 3 seconds. Further, when the tube is subjected to heat-treatment such as autoclave sterilization (121°C, 20 minutes), the cross section of the tube is easily deformed.

10 The tube is therefore poor in restoration capability after occlusion and heat resistance. Further, when the above content is less than 60 mass%, the resin composition has a high elastic modulus, and the tube has low flexibility, so that the tube is undesirably liable to keep on kinking or bending when bent.

15 Further, in the present invention, basically, the layer (II) to form a connection layer is a layer formed of a resin composition containing 45 to 100 mass% of the polypropylene resin (a) and 55 to 0 mass% of the copolymer (b).

20 The composition for the layer (II) can be determined to be optimum depending upon the object. That is, when the layer (II) is used as an outer layer, the content of the polypropylene resin (a) is at least 45 mass%. In this case, sticking of one tube to another during sterilization with high-pressure steam or sticking of the tube to a packing material can be prevented. When the multi-layered tube of the present invention is to be connected to other tube having a different diameter or to a part such as an injection-molded article with a solvent bonding or an adhesive bonding or by hot melt bonding, preferably, the content of the polypropylene resin (a) in the layer (II) to constitute a connection layer (outer layer and/or inner layer) is determined to be 70 mass% or less in view of adhesion capability.

35 When the layer (II) is used as an inner layer, the

content of the polypropylene resin (a) is determined to be at least 70 mass%. In this case, when the medical forceps is removed after the tube is closed with the forceps, the tube can restore its original form in a short period of time, and that the passage for a fluid can be secured. Further, when the multi-layered tube of the present invention is used in a way where it is being contact with blood like in a blood circuit or a blood tube, preferably, the content of the polypropylene resin (a) in the layer (II) that comes to be in contact with blood is at least 70 mass%, from the viewpoint of affinity to blood such as anti-coagulation of blood. As described above, the optimum composition for the layer (II) can be determined as required depending upon use.

In the present invention, the copolymer (b) is preferably the following hydrogenated block copolymer ((b1) - (b3)) or a hydrogenated polymer (b4).

In the copolymer (b), the content of the vinyl aromatic compound is preferably 10 to 40 mass%. When the content of the vinyl aromatic compound is less than 10 mass%, the tube sometimes has insufficient mechanical strength. When it exceeds 40 mass%, the composition has a high melt viscosity, so that the vinyl aromatic compound is poorly mixed with the polypropylene resin (a), which may impose limitations on molding.

In the isoprene polymer block (B) of the hydrogenated block copolymer (b1), preferably, the content of 1,2-bonds and 3,4-bonds (to be sometimes referred to as "vinyl bond content" hereinafter) is 10 to 75 mass%. When the vinyl bond content is too small, such a content is insufficient for transparency. When it is too large, the glass transition temperature of the resin composition comes to be too high, and the flexibility of a molded article from the resin composition is liable to be impaired. When the hydrogenation ratio of carbon-carbon double bonds in the copolymer (b1) is too small, the multi-layered tube tends to be poor in weatherability and heat resistance, so that the

above hydrogenation ratio is preferably at least 70 %. The reference to transparency is made above, since when the multi-layered tube of the present invention is used as a component of a medical device, it is desirable that the multi-layered tube has excellent transparency.

As the hydrogenated block copolymer (b2), it is preferred for the same reasons to use a hydrogenated block copolymer having an isoprene-butadiene copolymer block (C) having a 1,2-bond and 3,4-bond content of 20 to 85 % and having carbon-carbon double bonds at least 70 % of which are hydrogenated.

As the hydrogenated block copolymer (b3), it is also preferred for the same reasons to use a hydrogenated block copolymer having a butadiene polymer block (D) having a 1,2-bond content of at least 30 % and having carbon-carbon double bonds 70 % of which are hydrogenated.

In the copolymer (b), examples of the vinyl aromatic compound include styrene, α -methylstyrene, 1-vinylnaphthalene, 3-methylstyrene, 4-propylstyrene, 4-cyclohexylstyrene, 4-dodecylstyrene, 2-ethyl-4-benzylstyrene and 4-(phenylbutyl) styrene. Of these, styrene is particularly preferred.

Although not specially limited, the number average molecular weight of the polymer block (A) formed from the above vinyl aromatic compound is preferably in the range of from 2,500 to 20,000.

Although not specially limited, the number average molecular weight of each of the polymer blocks (B), (C) and (D) is preferably in the range of from 10,000 to 200,000. While the form of a polymer from isoprene and butadiene in the polymer block (C) is not specially limited, it may be any form of random, block and tapered forms.

In the copolymer (b), the form of bonding of each polymer block ((B), (C) or (D)) is not specially limited, and it may be linear, branched or any combination of these. Specific examples of the molecular structure of the copolymer

(b) include $P(QP)_n$ and $(PQ)_n$, in which P is the polymer block (A), Q is a polymer block (B), (C) or (D) and n is an integer of 1 or greater.

As the copolymer (b), further, there can be used a copolymer having a star-shaped molecular structure obtained in the presence of divinylbenzene, a tin compound or a silane compound as a coupling agent (e.g., a polymer represented by $[(PQ)_mX]$ in which P and Q are as defined above, m is an integer of 2 or greater and X is a residue of the coupling agent.

As the copolymer (b), copolymers having the above various molecular structures may be used alone, or two or more copolymers having the above various molecular structures such as a mixture of triblock type and diblock type copolymers may be used. The number average molecular weight of the above copolymer (b) is preferably in the range of from 30,000 to 300,000.

The method for producing the copolymer (b) can be selected from known production methods, and for example, there can be employed a method of hydrogenating a block copolymer obtained by any one of the following methods (α) to (γ), that is,

(α) a method in which a vinyl aromatic compound is polymerized in the presence of an alkyllithium compound as an initiator, and then a conjugated diene compound (isoprene, butadiene) and a vinyl aromatic compound are consecutively polymerized,

(β) a method in which a vinyl aromatic compound is polymerized, then a conjugated diene compound is polymerized, and the coupling of the resultant block copolymers is carried out in the presence of a coupling agent, and

(γ) a method in which a conjugated diene compound is polymerized in the presence of a dilithium compound as an initiator and then a vinyl aromatic compound is consecutively polymerized.

In the above method, the alkyllithium compound as an

initiator is selected from compounds whose alkyl group has 1 to 10 carbon atoms, and of these, methylolithium, ethyllithium, pentyllithium, n-butyllithium, s-butyllithium and t-butyllithium are preferred. Examples of the coupling agent for coupling the block copolymer include halogen compounds such as dichloromethane, dibromomethane, dichloroethane, dibromoethane, dibromobenzene and tin tetrachloride; ester compounds such as phenyl benzoate and ethyl acetate; divinylbenzene, and various silane compounds. Further, examples of the dilithium compound as an initiator include naphthalenedilithium and dilithiohexylbenzene.

The amount of the above initiator or the coupling agent is determined as required depending upon the molecular weight of a desired block copolymer. Per 100 parts by weight of all the entire monomers used for the polymerization, generally, the amount of the initiator is in the range of from 0.01 to 0.2 part by weight, and the amount of the coupling agent is in the range of from 0.04 to 0.8 part by weight.

The vinyl bond content in each of the polymer blocks (B) to (D) can be controlled by the use of a Lewis base as a cocatalyst in the polymerization. Examples of the above Lewis base include ethers such as dimethyl ether, diethyl ether and tetrahydrofuran; glycol ethers such as ethylene glycol dimethyl ether and diethylene glycol dimethyl ether; and amine-containing compounds such as triethylamine, N,N,N',N'-tetramethylethylenediamine (to be abbreviated as "TMEDA" hereinafter) and N-methylmorpholine. The Lewis base is used in such an amount that the molar amount of the Lewis base per mole of the lithium atom in the polymerization initiator is in the range of from 0.1 to 1,000 mol.

In the polymerization, it is preferred to use an organic solvent inert to the polymerization initiator as a solvent. The above solvent is preferably selected from aliphatic hydrocarbons having 6 to 12 carbon atoms such as hexane and heptane; alicyclic hydrocarbons such as

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In the multi-layered tube of the present invention, the layer (I) preferably has an elastic modulus (elastic modulus of the layer per se) of 30 MPa or less at 25°C. Further, each of the layer (I) and the layer (II) preferably has a haze of 25 % or less at the thickness of 1 mm. Further, preferably, the multi-layered tube of the present invention can form an arc having a radius of 20 mm without kinking.

The multi-layered tube of the present invention may be used as it is. Practically and preferably, however, the layer(s) (II) forming the outer surface and/or the inner surface of the multi-layered tube is/are used as connection layer(s), and other tube having a different diameter, a connector or a joint is connected thereto before use. The above connection is attained by solvent bonding or hot melt bonding, or may be attained by bonding with an adhesive.

Further, in the multi-layered tube of the present invention, preferably, the shear peel strength of the stuck portion (adhered portion) of outermost layers of the multi-layered tubes after autoclave sterilization at 121°C for 20 minutes is 35 N or lower, and the 180° peel strength of an stuck portion of the outermost layer and a polyolefin such as polypropylene forming the innermost layer after the sterilization is 5 N or lower. The term "180° peel strength" in the present invention refers to a strength measured by a test method defined in JIS K6854.

The multi-layered tube of the present invention is suitable as a medical tube for an extracorporeal circulation circuit, and, preferably, the multi-layered tube can form a through passage inside it within 3 seconds when it is closed with a medical tube forceps for 15 hours and then released from the forceps.

Each resin composition for constituting the multi-layered tube of the present invention may contain additives such as an antioxidant, an UV absorbent, a light stabilizer, a colorant, a crystal nucleating agent, etc., in such amounts that the properties of the multi-layered tube are not

impaired. Generally, the amount of these additives per 100 parts by mass are in the range of from 0.01 to 5 part by mass.

Each resin composition for constituting the multi-layered tube may contain other polymers such as hydrogenated
5 polyisoprene, hydrogenated polybutadiene, a hydrogenated styrene-isoprene random copolymer, butyl rubber, polyisobutylene, polybutene, ethylene-propylene rubber, an ethylene- α -olefin copolymer, an ethylene-vinyl acetate copolymer, an ethylene-methacrylic acid copolymer,
10 an ethylene-acrylic acid copolymer, ionomers of these, an ethylene-ethyl acrylate copolymer, an ethylene-methyl methacrylate copolymer, an ethylene-ethyl methacrylate copolymer, atactic polypropylene, and the like, in such amounts that the gist of the present invention is not
15 impaired. The above resin compositions may be crosslinked by a general crosslinking method using a peroxide, etc., before use.

The resin compositions for constituting the multi-layered tube of the present invention may be prepared by
20 kneading the polypropylene resin (a), the copolymer (b) and optionally the above additive(s) with a kneading machine such as a single-screw extruder, a twin-screw extruder, a kneader, a Banbury mixer, a roll, or the like. The thus-prepared resin compositions are formed into the multi-layered tube by
25 co-extrusion or coating.

The multi-layered tube of the present invention is excellent in flexibility, transparency, anti-kinking properties, restoration capability after occlusion and heat resistance. That is, specifically, ① when an optical bubble
30 detector is used, 1 mL single bubble is detected at a flow rate of 300 mL/minute, ② each of the compositions forming the layers has a haze of 25 % or less at the thickness of 1 mm, ③ when the multi-layered tube is formed into an arc having a radius of 20 mm, it is not bent, ④ when the multi-
35 layered tube is closed with a medical tube forceps for 15 hours and then released from the forceps, the tube forms a

through passage inside within 3 seconds, and ⑤ after the multi-layered tube is sterilized in an autoclave (121°C, 20 minutes), the shear peel strength of the stuck portion of the outermost layers of the multi-layered tubes is 35 N or lower, and the 180° peel strength of an stuck portion of the outermost layer of the tube and a sterilization bag having the innermost layer formed of polypropylene is 5 N or lower.

One example of the embodiment of the present invention will be explained with reference to attached drawings hereinafter. Fig. 1 shows cross-sectional views of multi-layered tubes of the present invention. Figs. 2 and 3 are partially enlarged longitudinal sectional views of medical device comprising the multi-layered tube of the present invention connected to other connection members such as other tube having a different diameter and an injection-molded article. In addition, the injection-molded article in the present invention refers to a tubular member connectable to the multi-layered tube of the present invention and includes, for example, a connector and a joint.

In Fig. 1(1), a multi-layered tube 1 is a dual layered tube formed of the layer (I) forming an inner layer 3 and the layer (II) forming an outer layer 5. In Fig. 1(2), a multi-layered tube 1 is a dual layered tube formed of the layer (I) forming an outer layer 5 and the layer (II) forming an inner layer 3. In Fig. 1(3), further, a multi-layered tube 1 is a three-layered tube formed of the layer (I) forming an intermediate layer 7 and the layers (II) forming an inner layer 3 and an outer layer 5.

Fig. 2 shows a state in which the dual layered tube 1 shown in Fig. 1(1) is connected to a connection member 50 such as other tube having a different diameter or an injection-molded article, and the layer (II) forming the outer layer 5 and an inner wall surface 55 of the connection member 50 can be connected to each other. The term "connection" means connection with a solvent bonding or hot melt bonding as already described. The adhesion by hot melt

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bonding includes application of a hot melt bonding using electric heat, high-frequency hot melt bonding and hot melt bonding by heating with hot air. However, the bonding shall not be limited thereto, and other hot melt bonding may be employed. Fig. 3 also shows a state where the dual tube shown in Fig. 1(2) and the connection member 50 are connected to each other, and the layer (II) forming the inner layer 3 and an outer wall surface 57 of the connection member 50 are connected to each other similarly with a solvent bonding or by hot melt bonding.

In the dual layered tube, the thickness ratio of the layer (I) and the layer (II), layer (I)/layer (II), is preferably $940 - 980/60 - 20$. That is because the entire tube is imparted with flexibility and anti-kinking properties by allowing the layer (I) to have a sufficient thickness as compared with the layer (II). That is, when the thickness ratio of the layer (I) is less than 940 (when the thickness ratio of the layer (II) exceeds 60), the wall thickness of the tube is small and kinking is liable to occur. When the thickness ratio of the layer (I) exceeds 980 (when the thickness ratio of the layer (II) is less than 20), the tube wall thickness is extremely large, and the rigidity is too large, so that the tube is liable to have decreased flexibility. Further, the thickness of the layer (II) is too small, and the tube tends to be no longer suitable for application of solvent bonding or hot melt bonding.

In the three-layered tube, the thickness ratio of the layer (I) and the layers (II), layer (II)/layer (I)/layer (II), is preferably $20 - 30/940 - 960/20 - 30$. When the thickness ratio of the layer (I) is less than 940 (when the thickness ratio of the layer(s) (II) exceeds 30), the tube wall thickness is too small, and kinking is liable to occur. When the thickness ratio of the layer(s) (II) is less than 20 (when the thickness ratio of the layer (I) exceeds 960), the thickness of the layer (II) is too small, so that it is difficult to apply solvent bonding or hot melt bonding.

When the multi-layered tube of the present invention as a component is connected to a member such as other tube having a different diameter or an injection-molded article as described above, it can suitably form medical devices such as a blood circuit, a blood bag, a catheter, or the like.

The multi-layered tube of the present invention makes the best use of the above properties and can be used in an extracorporeal circulation circuit such as a blood circuit for artificial kidney dialysis, a blood circuit for blood plasma exchange, a circuit for ascites treatment systems by filtration, concentration and infusion, or the like. Further, in addition to the above extracorporeal circulation circuit, the multi-layered tube of the present invention can be used, for example, in various medical devices such as a blood tube, an infusion tube, a catheter, a balloon catheter, etc., industrial uses such as a hose, fields in agricultures, forestry and fisheries and the field of household articles, where excellent flexibility and transparency are required.

Examples

The present invention will be explained with reference to Examples hereinafter, in which "%" stands for "mass%" unless otherwise specified.

In the following Referential Examples 1 and 2, Examples 1 to 5 and Comparative Example 1, multi-layered tubes were evaluated for sticking of tubes to each other during sterilization, anti-kinking properties and adhesion by the following methods.

(Sticking during sterilization)

Tubes were fixed with a paper tape so as to intimately adhere to each other, and the tubes were sterilized in an autoclave at 121°C for 20 minutes and then measured for a shear peel resistance.

(Kinking occurrence radius)

Both ends of a 20 cm long tube were fixed to tools, the distance between the tools was gradually decreased,

dimensions were taken when the tube was bent, and a radius of curvature was calculated.

(Solvent bonding properties)

A tube that had an internal diameter of 6.8 mm and was prepared from the same composition as that of an adhesive layer was used for bonding with THF, and after 24 hours, the tube was measured for a tensile strength.

Referential Example 1 (Determination of amount ratio for layer (II))

For the layer (II), polypropylene (F327) and a styrene-isoprene-styrene hydrogenated block copolymer (HVS-3) were mixed in amount ratios shown in Table 1 to prepare a tube having an outer diameter of 6.8 mm, and the tube was measured for sticking strength during sterilization and strength of solvent bonding. Table 1 shows the results.

Table 1

Amount ratio of PP (a)/Copolymer (b)	Sticking strength of one tube to another	Strength of bonding to tube having a different diameter
100/0	No sticking	6 N
70/30	Less than 10 N	90 N
50/50	34 N	97 N
40/60	36 N	105 N

According to the results in Table 1, when the amount ratio of the polypropylene resin (a), in the amount ratio of the polypropylene resin (a) and the copolymer (b), is 70 or less (when the amount ratio of the copolymer (b) is 30 or greater), the bonding strength of the tube to the tube having a different diameter is good. However, when the amount ratio of the polypropylene resin (a) is 40 or less (when the amount ratio of the copolymer (b) is 60 or greater), undesirably, the sticking strength of the tubes to each other comes to be

36 N or more.

When the amount ratio of the polypropylene resin (a) exceeds 70 (when the amount ratio of the copolymer (b) is less than 30), the sticking of the tubes to each other is desirably less than 10 N. Undesirably, however, the bonding strength to the tube having a different diameter is less than 90 N.

It is therefore seen that the polypropylene resin (a)/copolymer (b) amount ratio is preferably determined to be 70/30 to 45/55 for preventing the sticking of tubes to one another during sterilization and maintaining the strength of solvent bonding to a tube having a different diameter.

Examples 1 - 5 and Comparative Example 1

A commercially available polypropylene [F327 (trade name), supplied by Grand Polymer Inc., flexural modulus (JIS K7203): 780 MPa] was used as a polypropylene resin (a), and a commercially available hydrogenated styrene-ethylene-butylene-styrene block copolymer [Kraton G 61652 (trade name), supplied by Shell Chemical Co.], a hydrogenated isoprene copolymer [Hybrar HVS-3 (trade name), supplied by Kuraray Ltd.] or a hydrogenated styrene-butadiene rubber [DYNARON 1320P (trade name), supplied by JSR] was used as a copolymer (b).

The above polypropylene resin (a) and the copolymer (b) were mixed in a mixing ratio shown in Table 2, to prepare a resin composition.

The above resin compositions were co-extruded to form a three-layered tube having a layer (II) (outer layer)/layer (I) (intermediate layer)/layer (II) (inner layer) structure.

The three-layered tube has a size of 7 mm as an outer diameter and 1 mm as a wall thickness, and the thickness ratio of the layer (I) and the layers (II) were as shown in Table 2.

The above multi-layered tube was measured for

stickiness of tubes to each other during sterilization, anti-kinking properties and bonding properties, and Table 2 shows the results.

As is clearly shown in Table 2, the three-layered tubes of Examples 1 to 5 according to the present invention nearly satisfy the formerly described performances (a) to (c) which a medical tube is required to have. In contrast, when the amount ratio of the polypropylene is decreased and the amount ratio of the copolymer (b) is increased in the composition for the layers (II) like Comparative Example 1, the sticking during sterilization increases.

In Referential Examples 2 to 4, Examples 6 to 16 and Comparative Examples 2 and 3, polymers were measured for styrene contents, number average molecular weights, vinyl bond contents and hydrogenation ratios, molded articles from resin compositions were measured for flexibility and transparency, and tubes were measured for transparency, anti-kinking properties, restoration capability after occlusion and heat resistance, by the following methods.

(Styrene content)

Calculated on the basis of mass of each monomer used for polymerization.

(Number average molecular weight)

A number average molecular weight (Mn) as polystyrene was determined by GPC measurement.

(Vinyl bond content)

A block copolymer before hydrogenation was dissolved in deuterated chloroform (CDCl_3) and measured for $^1\text{H-NMR}$ spectrum, and a vinyl bond content was calculated on the basis of sizes of peaks corresponding to 1,2-bonds and 3,4-bonds.

(Hydrogenation ratio)

Hydrogenation ratio was calculated on the measurement of iodine numbers of the block copolymer before and after hydrogenation.

Table2

		Example 1	Example 2	Example 3
Amount ratio (%)	Layer (I)	(a) PPF327 20% (b) KratonGG1 652 80%	(a) PP F327 20% (b) Hybrar HVS-3 80%	(a) PP F327 20% (b) DYNARON 1320P 80%
	Layer (II)	(a) PPF327 50% (b) KratonGG1 652 50%	(a) PP F327 50% (b) Hybrar HVS-3 50%	(a) PP F327 50% (b) DYNARON 1320P 50%
Thickness ratio	Layer (I)	940	940	940
	Layer (II)	30×2	30×2	30×2
Sticking during sterilization		3~3.4	3~3.4	3~3.5
Radius when kinking occurred		17 mm	17mm	16mm
Solvent bonding properties		90~120N	90~120N	90~110N
		Example 4	Example 5	Comparative Example 1
Amount ratio (%)	Layer (I)	(a) PP F327 20% (b) Hybrar HVS-3 80%	(a) PP F327 20% (b) KratonGG1652 80%	(a) PP F327 20% (b) Hybrar HVS-3 80%
	Layer (II)	(c) PP F327 50% (d) Hybrar HVS-3 50%	(a) PP F327 100%	(a) PP F327 40% (b) Hybrar HVS-3 60%
Thickness ratio	Layer (I)	800	940	940
	Layer (II)	100×2	30×2	30×2
Sticking during sterilization		3~3.4	No sticking	3.4~3.8
Radius when kinking occurred		23mm	37mm	17mm
Solvent bonding properties		90~110N	Less than 10N	90~110N

(Flexibility of resin composition)

A test piece having a length of 30 mm, a width of 5 mm and a thickness of 1 mm was prepared, and measured for a dynamic viscoelasticity dependent upon temperatures. The elastic modulus at 25°C was employed. Measurement conditions were as follows. Tensile mode (sine wave distortion, amplitude displacement; 10 μ m, frequency; 1Hz), a chuck-chuck distance; 20 mm, measurement temperature range; -100 - 150°C, a temperature elevation rate; 3°C/minute

(Transparency of resin composition)

A sheet having a thickness of 1 mm was prepared, and measured for a haze value with a haze meter according to a method defined in JIS K7105, and the haze value was used as an index for transparency of a resin composition.

(Transparency of tube)

When a tube was filled with water, a degree to which air bubbles inside the tube were visually observed was used as an index for transparency.

(Anti-kinking properties of tube)

A tube having a length of 20 cm was bent in the form of a U-letter and left as it was for approximately 1 minute, and then the tube was observed for a kinking. The tube was measured for a radius of curvature with an R gage, and a smallest radius of curvature at which no kinking occurred was used as an index for anti-kinking properties.

(Restoration capability of tube after occlusion)

A tube filled with a saline solution was closed with a medical tube forceps for 15 hours, and then the forceps was removed. A time period was measured before the tube formed a through passage inside and used as an index for restoration capability of tube after occlusion.

(Resistance against tube/tube sticking under heat)

Two tubes having a length of 10 cm each were stacked such that 5 cm each of them were stacked one on the other in parallel, and the stacked portions were bound with a paper tape. The tubes were subjected to autoclave sterilization

(121°C, 20 minutes), and the binding paper tape was removed. The tubes were measured for a shear peel strength, and the tube/tube sticking strength was used as an index for resistance against sticking under heat. As a shear peel strength, a maximum value obtained under conditions of a test speed of 100 mm/minute with a tensile tester was employed. (Resistance against tube/film sticking under heat)

A tube having a length of 10 cm was placed in a sterilization bag (supplied by Hoky Medical Co.) and subjected to autoclave sterilization (121°C, 20 minutes). Then, the film was measured for a 180° peel strength, and the tube/film sticking was used as an index for resistance against sticking under heat. As a shear peel strength, an average value obtained under conditions of a test speed of 100 mm/minute with a tensile tester was employed.

Referential Example 2 (Preparation of Copolymer No. 1)

In a pressure vessel where dry nitrogen had been substituted, styrene was polymerized at 60°C in cyclohexane as a solvent in the presence of s-butyllithium as a polymerization initiator, and then TMEDA was added as a Lewis base. Then, isoprene and styrene were consecutively polymerized to give a styrene-isoprene-styrene block copolymer. The thus-obtained block copolymer was hydrogenated in cyclohexane in the presence of Pd/C as a catalyst under a 2 MPa hydrogen atmosphere, to give a hydrogenated block copolymer (the hydrogenated block copolymer obtained in Referential Example 2 will be abbreviated as "Copolymer No. 1" hereinafter). Table 3 shows a styrene content, a number average molecular weight, a vinyl bond content and a hydrogenation ratio of the obtained Copolymer No. 1.

Referential Example 3 (Preparation of Copolymer No. 2)

Styrene, a mixture of isoprene with butadiene [isoprene/butadiene = 60/40 (mass ratio)] and styrene were

consecutively polymerized in a cyclohexane solvent in the presence of s-butyllithium and TMEDA in the same manner as in Referential Example 2, to give a styrene-
 (isoprene/butadiene)-styrene block copolymer. The thus-
 obtained block copolymer was hydrogenated in the same manner
 as in Referential Example 2, to give a hydrogenated block
 copolymer (the hydrogenated block copolymer obtained in
 Referential Example 3 will be abbreviated as "Copolymer No.
 2" hereinafter). Table 3 shows a styrene content, a number
 average molecular weight, a vinyl bond content and a
 hydrogenation ratio of the obtained Copolymer No. 2.

Referential Example 4 (Preparation of Copolymer No. 3)

Styrene, butadiene and styrene were consecutively
 polymerized in a cyclohexane solvent in the presence of s-
 butyllithium and TMEDA in the same manner as in Referential
 Example 2, to give a styrene-butadiene-styrene block
 copolymer. The thus-obtained block copolymer was
 hydrogenated in the same manner as in Referential Example 2,
 to give a hydrogenated block Copolymer No. 3 (the
 hydrogenated block copolymer obtained in Referential Example
 4 will be abbreviated as "Copolymer No. 3" hereinafter).
 Table 3 shows a styrene content, a number average molecular
 weight, a vinyl bond content and a hydrogenation ratio of the
 obtained Copolymer No. 3.

Table3

	Copolymer No.	Molecular structure before hydrogen- ation (Note)	Styrene content (%)	Number average molecular weight ($\times 10^4$)	Vinyl bond content (mol%)	Hydrogen- ation ratio (%)
REx. 2	1	A-B-A	20	10.3	55	80
REx. 3	2	A-C-A	20	10.8	60	82
REx. 4	3	A-D-A	20	10.5	72	83

(Note) A: Polystyrene block
B: Polyisoprene block
C: Poly(isoprene/butadiene) block
D: Polybutadiene block

Examples 6 - 9 and Comparative Examples 2 - 3

As a polypropylene resin (a), a commercially available block type polypropylene [BC1B (trade name), supplied by Nippon Polychem.], a random type polypropylene [J215W (trade name), supplied by Grand Polymer Co.] and a homo type polypropylene [MA3 (trade name), supplied by Nippon Polychem.] were used. As a copolymer (b), Copolymer No. 1 obtained in Referential Example 2, Copolymer No. 2 obtained in Referential Example 3, Copolymer No. 3 obtained in Referential Example 4 and a commercially available hydrogenated styrene-butadiene rubber [DYNARON 1320P (trade name), supplied by JSR Co.,Ltd] were used.

The polypropylene resin (a) and the copolymer (b) were kneaded in an amount ratio (ratio by mass) shown in Table 4 at 230°C in a twin-screw extruder, to give resin compositions.

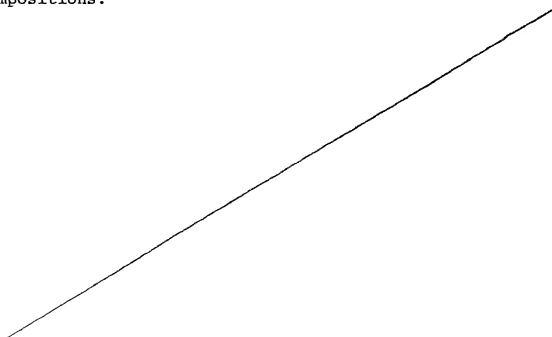


Table4

	Example6	Example7	Example8	Example9
Layer (I) (Thickness1mm)	(a)PP BC1B(5%) (b)CopolymerNo.1(95%)	(a)PP J215W(40%) (b)CopolymerNo.2(60%)	(a)PP J215W(20%) (b)CopolymerNo.3(80%)	(a)PP MA3(30%) (b)DYNARON 1320P(70%)
Layer (II), inner layer (Thickness30 μm)	(a)PP BC1B(90%) (b)CopolymerNo.1(10%)	None	None	None
Layer (II), outer layer (Thickness30 μm)	None	(a)PP J215W(80%) (b)CopolymerNo.2(20%)	(a)PP J215W(50%) (b)CopolymerNo.3(50%)	(a)PP MA3(100%)
Flexibility of tube ^{*1}	⊙	○	⊙	⊙
Elastic modulus of layer(I)	8.5MPa	50MPa	11MPa	15MPa
Transparency of tube ^{*2}	○	○	○	○
Haze of layer(I)(%)	2%	5%	4%	4%
Haze of layer(II)(%)	20%	16%	7%	25%
Anti-kinking properties ^{*3}	○ 12mm	○ 12mm	○ 11mm	○ 13mm
Remarks	None	None	None	None
	Comparative example2	Comparative example3		
Layer (I) (Thickness1mm)	(a)PP BC1B(3%) (b)CopolymerNo.1(97%)	(a)PP J215W(50%) (b)CopolymerNo.2(50%)		
Layer (II), inner layer (Thickness30 μm)	(a)PP BC1B(90%) (b)CopolymerNo.1(10%)	None		
Layer (II), outer layer (Thickness30 μm)	None	(a)PP J215W(80%) (b)CopolymerNo.2(20%)		
Flexibility of tube ^{*1}	⊙	×		
Elastic modulus of layer(I)	8MPa	100MPa		
Transparency of tube ^{*2}	○	○		
Haze of layer(I)(%)	1%	7%		
Haze of layer(II)(%)	20%	16%		
Anti-kinking properties ^{*3}	○ 12mm	○ 15mm		
Remarks	Cross section of tube deformed to oval	deficient in flexibility		

(Notes) *1: Evaluation of flexibility of tube was based on elastic modulus of layer (I); ⊙: less than 30 MPa, ○: 30 - 100 MPa, ×: over 100 MPa

*2: Evaluation base of transparency of tube: ○ Air bubbles were recognizable, ×: No air bubble was recognizable.

*3: Evaluation of anti-kinking properties of tube was based on maximum diameter at which kinking occurred; ○: less than 20 mm, ×: over 20 mm

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The obtained resin compositions were formed at 230°C into a dual layer tube having an outer diameter of 5.6 mm and an inner diameter of 3.3 mm, and the dual tube was evaluated for flexibility, transparency, anti-kinking properties, resistance against sticking under heat and restoration capability after occlusion. Table 4 shows the results.

It is seen from Table 4 that the multi-layered tubes of Examples 6 to 9 are excellent in flexibility, transparency and anti-kinking properties, but that when the amount ratio of the polypropylene resin in the layer (I) is small like Comparative Example 2, it is difficult to form a tube and the cross section of the tube is deformed. Further, when the amount ratio of the polypropylene resin in the layer (I) is large like Comparative Example 3, the flexibility of the tube is deficient.

Examples 10 - 13

A commercially available random type polypropylene [J215W (trade name), supplied by Grand Polymer Co.] was used as a polypropylene resin (a), and copolymer No. 1 obtained in Referential Example 2 was used as a copolymer (b).

The above polypropylene resin (a) and the copolymer (b) were kneaded in an amount ratio (ratio by mass) shown in Table 5 at 230°C in a twin-screw extruder, to give a resin composition. The obtained resin compositions were formed at 230°C into a three-layered tube having an outer diameter of 5.6 mm and an inner diameter of 3.3 mm as shown in Fig. 1(3), and the three-layered tube was evaluated for flexibility, transparency, anti-kinking properties, resistance against sticking under heat and restoration capability after occlusion. Table 5 shows the results. It is seen from Table 5 that the multi-layered tubes in Examples 10 to 13 are excellent in flexibility, transparency, anti-kinking properties, resistance against sticking under heat and restoration capability after occlusion.

Example 14

A dual layered tube having an outer diameter of 8 mm and an inner diameter of 6 mm was prepared in the same manner as in Example 8, and a three-layered tube having an outer diameter of 6 mm and an inner diameter of 4 mm was prepared in the same manner as in Example 10. These tubes were connected by solvent bonding using tetrahydrofuran. The bonded portion had a tensile bonding strength of 130 N, or attained strong connection.

Table5

	Table10	Table11	Table12	Table13
Layer (I) (Thickness1mm)	(a)PP J215W(20%) (b)CopolymerNo.1(80%)	(a)PP J215W(20%) (b)CopolymerNo.1(80%)	(a)PP J215W(20%) (b)CopolymerNo.1(80%)	(a)PP J215W(20%) (b)CopolymerNo.1(80%)
Layer (II) ,inner layer (Thickness30 μm)	(a)PP J215W(60%) (b)CopolymerNo.1(40%)	(a)PP J215W(60%) (b)CopolymerNo.1(40%)	(a)PP J215W(40%) (b)CopolymerNo.1(60%)	(a)PP J215W(100%)
Layer (II') ,outer layer (Thickness30 μm)	(a)PP J215W(50%) (b)CopolymerNo.1(50%)	(a)PP J215W(40%) (b)CopolymerNo.1(60%)	(a)PP J215W(70%) (b)CopolymerNo.1(30%)	(a)PP J215W(60%) (b)CopolymerNo.1(40%)
Flexibility of tube ^{*1}	◎	◎	◎	◎
Elastic modults of layer(I)	12MPa	12MPa	12MPa	12MPa
Transparency of tube ^{*2}	○	○	○	○
Haze of layer (I) (%)	3%	3%	3%	3%
Haze of layer(II) (%)	11%	11%	5%	25%
Haze of layer (II') (%)	7%	5%	14%	11%
Anti-kinking properties ^{*3}	○ 12mm	○ 11mm	○ 15mm	○ 13mm
Resistance against sticking under heat [*]	◎	○	◎	◎
Shear peel strenght Tube / tube	34N	37N	14N	20N
180° Peel strenght Tube / film	2N	10N	1N	2N
Restoration capability after occlusion ^{*5} Remarks	○ 3 seconds None	○ 3 seconds None	○ 15 seconds None	◎ 2 seconds None

(Notes) *1: Evaluation of flexibility of tube was based on elastic modulus of layer (I); ⊙: less than 30 MPa, ○: 30 - 100 MPa, ×: over 100 MPa

*2: Evaluation base of transparency of tube: ○ Air bubbles were recognizable, ×: No air bubble was recognizable.

*3: Evaluation of anti-kinking properties of tube was based on maximum diameter at which kinking occurred; ○: less than 20 mm, ×: 20 mm or more

*4: Evaluation of resistance against sticking under heat was based on shear peel strength of tube/tube sticking; ⊙: less than 35 N, ○: 35 - 40 N, ×: over 40 N and also based on 180° peel strength; ○: less than 10 N, ×: 10 N or more

*5: Evaluation of restoration capability after occlusion was based on time period for which through passage was formed; ⊙: less than 3 seconds, ○: 3 - 120 seconds, ×: over 120 seconds

Example 15

The three-layered tube prepared in Example 10 was used to obtain a blood circuit for dialysis. The three-layered tube was strongly connected to a connector. A three-layered tube portion of the blood circuit was closed with a medical tube forceps for 15 hours, and then the forceps was removed. The tube formed a through passage inside within 3 seconds after the removal. The above three-layered tube is excellent in flexibility, transparency, anti-kinking properties, restoration capability after occlusion and resistance against sticking under heat, and it is shown that it is at a practical level when it is used in a medical device or a medical tube, particularly, a circuit for extracorporeal circulation.

Comparative Example 4

A commercially available polypropylene [F327 (trade name)], supplied by Grand Polymer Co.] was used as a

polypropylene resin (a), Copolymer No. 1 obtained in Referential Example 2 was used as a copolymer (b), and these were used for a layer (I) (intermediate layer) and a layer (II) as an outer layer. A high-density polyethylene [HJ490 (trade name), supplied by Japan Polychem Co.] was used for a layer (II) as an inner layer. And, a three-layered tube having a constitution shown in Table 6 was prepared. When the three-layered tube was closed with a forceps for 15 hours after sterilization with high-pressure steam, the time period before the formation of a through passage was 120 seconds or longer.

Table 6

	Comparative Example 4
Layer (I) (thickness 1 mm)	(a) PP F327 (30 %) (b) copolymer No. 1 (70 %)
Layer (II), inner layer (thickness 30 μ m)	High-density polyethylene HJ490
Layer (II), outer layer (thickness 30 μ m)	(a) PP F327 (50 %) (b) copolymer No. 1 (50 %)

Industrial Utility

According to the present invention, there is provided a multi-layered tube that is excellent in flexibility, transparency, anti-kinking properties, restoration capability after occlusion, heat resistance, resistance against sticking under heat and bonding properties, and which is free from elution of a plasticizer and generates no toxic gas when incinerated.

The multi-layered tube of the present invention can be used as it is or can be used as a component of medical devices such as a blood tube, a blood bag, an medical solution bag, an infusion tube, a blood circuit, a catheter, etc., and particularly for a circuit for extracorporeal

circulation. Further, it is not limited to medical applications, but can be applied to various fields such as industrial fields and fields of general household articles.

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CLAIMS

1. A multi-layered tube composed of at least two layers, wherein at least one layer of said layers is a layer (I) made of a resin composition comprising 5 to 40 mass% of a polypropylene resin (a), and 95 to 60 mass% of at least one copolymer (b) selected from the group consisting of

a hydrogenated block copolymer (b1) obtained by hydrogenating a block copolymer formed of a polymer block (A) from a vinyl aromatic compound and an isoprene polymer block (B),

a hydrogenated block copolymer (b2) obtained by hydrogenating a block copolymer formed of a polymer block (A) from a vinyl aromatic compound and a polymer block (C) from isoprene and butadiene,

a hydrogenated block copolymer (b3) obtained by hydrogenating a block copolymer formed of a polymer block (A) from a vinyl aromatic compound and a butadiene polymer block (D), and

a hydrogenated copolymer (b4) obtained by hydrogenating a copolymer of a vinyl aromatic compound and butadiene, and

at least one layer of the remaining layer or layers is a layer (II) formed of a resin composition comprising 45 to 100 mass% of a polypropylene resin (a) and 55 to 0 mass% of the above copolymer (b), and

further wherein said layer (I) forms one layer of an inner layer and an outer layer and said layer (II) forms the other layer, or said layer (I) forms an intermediate layer and the layer (II) forms the inner layer and the outer layer.

2. The multi-layered tube of claim 1, where the tube is a dual layered tube, and said layer (I) forms an inner layer and said layer (II) forms an outer layer, or the layer (I) forms an outer layer and the layer (II) forms an inner layer.

3. The multi-layered tube of claim 2, wherein said dual layered tube has a layer (I)/layer (II) thickness ratio of 940 - 980/60 - 20.

5

4. The multi-layered tube of any one of claims 1 to 3, wherein said layer (II) is a layer (II-1) formed of a resin composition containing 45 to 70 mass% of the polypropylene resin (a) and 55 to 30 mass% of the copolymer (b).

10

5. The multi-layered tube of any one of claims 1 to 3, wherein said layer (II) is a layer (II-2) formed of a resin composition containing 70 to 100 mass% of the polypropylene resin (a) and 30 to 0 mass% of the copolymer (b).

15

6. The multi-layered tube of claim 1, Wherein the tube is a three-layered tube, and said layer (I) forms an intermediate layer and said layer (II) forms an inner layer and an outer layer.

20

7. The multi-layered tube of claim 6, wherein the tube has an outer layer/intermediate layer/inner layer thickness ratio of 20 - 30/940 - 960/20 - 30.

25

8. The multi-layered tube of claim 6 or 7, wherein said layer (II) is a layer (II-1) formed of a resin composition containing 45 to 70 mass% of the polypropylene resin (a) and 55 to 30 mass% of the copolymer (b).

30

9. The multi-layered tube of any one of claims 6 to 8, wherein, in the said three-layered tube, said outer layer is a layer (II-1) formed of a resin composition containing 45 to 70 mass% of the polypropylene resin (a) and 55 to 30 mass% of the copolymer (b),

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said intermediate layer is the layer (I) formed of a resin composition containing 5 to 40 mass% of the

polypropylene resin (a) and 95 to 60 mass% of the copolymer (b), and

said inner layer is a layer (II-2) formed of a resin composition containing 70 to 100 mass% of the polypropylene resin (a) and 30 to 0 mass% of the copolymer (b).

10. The multi-layered tube of any one of claims 1 to 9, wherein said hydrogenated block copolymer (b1) has a vinyl aromatic compound component content of 10 to 40 mass%, the isoprene polymer block (B) has a 1,2-bond and 2,4-bond content of 10 to 75 mol%, and at least 70 % of carbon-carbon double bonds of the block copolymer (b1) are hydrogenated.

11. The multi-layered tube of any one of claims 1 to 9, wherein said hydrogenated block copolymer (b2) has a vinyl aromatic compound component content of 10 to 40 mass%, the polymer block (C) has an isoprene component/butadiene component weight ratio of 5/95 to 95/5 and a 1,2-bond and 3,4-bond content of 20 to 85 mol%, and at least 70 % of carbon-carbon double bonds of the block copolymer (b2) are hydrogenated.

12. The multi-layered tube of any one of claims 1 to 9, wherein said hydrogenated block copolymer (b3) has a vinyl aromatic compound component content of 10 to 40 mass%, the butadiene polymer block (D) has a 1,2-bond content of at least 30 mol%, and at least 70 % of carbon-carbon double bonds of the block copolymer (b3) are hydrogenated.

13. The multi-layered tube of any one of claims 1 to 12, wherein said vinyl aromatic compound is styrene.

14. The multi-layered tube of any one of claims 1 to 13, wherein said tube is a multi-layered tube for medical use.

15. The multi-layered tube of claims 14, wherein said

tube is for forming a circuit for extracorporeal circulation.

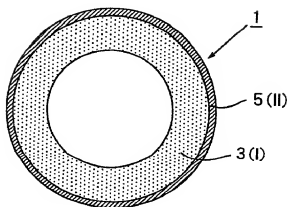
16. The multi-layered tube of any one of claims 1 to 15,
wherein the polypropylene resin (a) forming said layer (I)
5 has a bending flexural modulus of 200 to 400 MPa and the
polypropylene resin (a) forming said layer (II) has a
flexural modulus of 500 to 900 MPa.

17. A medical device comprising the multi-layered tube
10 recited in any one of claims 1 to 16 and other member to
which said multi-layered tube is connected.

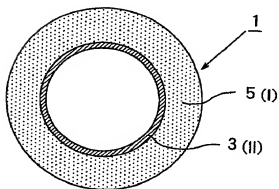
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Fig.1

(1)



(2)



(3)

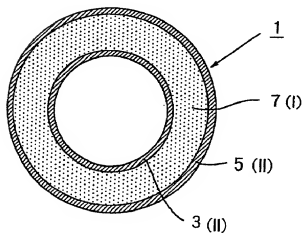


Fig.2

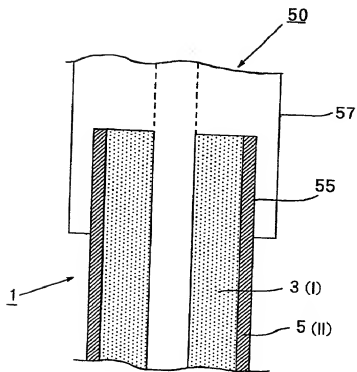
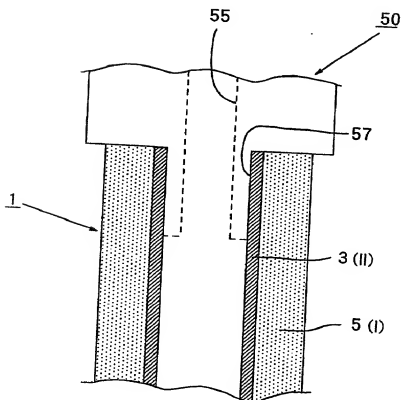


Fig.3



Declaration and Power of Attorney For Patent Application

特許出願宣言書及び委任状

Japanese Language Declaration

日本語宣言書

下記の氏名の発明者として、私は以下の通り宣言します。

As a below named inventor, I hereby declare that:

私の住所、私書箱、国籍は下記の私の氏名の後に記載された通りです。

My residence, post office address and citizenship are as stated next to my name.

下記の名称の発明に関して請求範囲に記載され、特許出願している発明内容について、私が最初かつ唯一の発明者（下記の氏名の一つの場合）もしくは最初かつ共同発明者（下記の名称が複数の場合）であると信じています。

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled.

Multi-layered Tube And Medical Device

Comprising Multi-layered Tube

上記発明の明細書は、

☐ 本書に添付されています。

the specification of which

☒ is attached hereto.
☒ was filed on September 22, 2000

☐ 月 日 に提出され、米国出願番号または特許協定条

as United States Application Number or
PCT International Application Number
PCT/JP00/06493 and was amended on
_____ (if applicable).

☐ 約国際出願番号を _____ とし、
(該当する場合) _____ に訂正されました。

私は、特許請求範囲を含む上記訂正後の明細書を検討し、内容を理解していることをここに表明します。

I hereby state that I have reviewed and understand the contents of the above identified specification, including the claims, as amended by any amendment referred to above.

私は、連邦規則法典第37編第1条56項に定義されるとおり、特許資格の有無について重要な情報を開示する義務があることを認めます。

I acknowledge the duty to disclose information which is material to patentability as defined in Title 37, Code of Federal Regulations, Section 1.56.

Japanese Language Declaration

(日本語宣言書)

私は、米国法典第35編119条 (a) - (d) 項又は365条 (b) 項に基づき下記の、米国以外の国の少なくとも一カ国を指定している特許協力条約365 (a) 項に基づく国際出願、又は外国での特許出願もしくは発明者証の出願についての外国優先権をここに主張するとともに、優先権を主張している、本出願の前に出願された特許または発明者証の外国出願を以下に、枠内をマークすることで、示しています。

Prior Foreign Application(s)

外国での先行出願

120270/2000

(Number)
(番号)

Japan

(Country)
(国名)

(Number)
(番号)

(Country)
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私は、第35編米国法典119条 (e) 項に基づいて下記の米国特許出願規定に記載された権利をここに主張いたします。

(Application No.)
(出願番号)

(Filing Date)
(出願日)

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(Application No.)
(出願番号)

(Filing Date)
(出願日)

(Application No.)
(出願番号)

(Filing Date)
(出願日)

私は、私自信の知識に基づいて本宣言書中で私が行なう表明が真実であり、かつ私の入手した情報と私の信じるところに基づく表明が全て真実であると信じていること、さらに故意になされた虚偽の表明及びそれと同等の行為は米国法典第18編1001条に基づき、罰金または拘禁、もしくはその両方により処罰されること、そしてそのような故意による虚偽の声明を行なえば、出願した、又は既に許可された特許の有効性が失われたことを認識し、よってここに上記のごとく宣誓を致します。

I hereby claim foreign priority under Title 35, United States Code, Section 119 (a)-(d) or 365(b) of any foreign application(s) for patent or inventor's certificate, or Section 365(a) of any PCT International application which designated at least one country other than the United States, listed below and have also identified below, by checking the box, any foreign application for patent or inventor's certificate, or PCT International application having a filing date before that of the application on which priority is claimed.

Priority Claimed

優先権主張

☒ Yes ☐ No

はい いいえ

☐ Yes ☐ No

はい いいえ

21/April/2000

(Day/Month/Year Filed)
(出願年月日)

(Day/Month/Year Filed)
(出願年月日)

I hereby claim the benefit under Title 35, United States Code, Section 119(e) of any United States provisional application(s) listed below.

(Application No.)
(出願番号)

(Filing Date)
(出願日)

I hereby claim the benefit under Title 35, United States Code, Section 120 of any United States application(s), or Section 365(c) of any PCT International application designating the United States, listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States or PCT International application in the manner provided by the first paragraph of Title 35, United States Code Section 112, I acknowledge the duty to disclose information which is material to patentability as defined in Title 37, Code of Federal Regulations, Section 1.56 which became available between the filing date of the prior application and the national or PCT International filing date of application.

(Status: Patented, Pending, Abandoned)
(現況: 特許許可済、係属中、放棄済)

(Status: Patented, Pending, Abandoned)
(現況: 特許許可済、係属中、放棄済)

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Japanese Language Declaration
(日本語宣言書)

委任状: 私は下記の発明者として、本出願に関する一切の手続きを米特許商標局に対して遂行する弁理士または代理人として、下記の者を指名いたします。
(弁理士、または代理人の指名及び登録番号を明記のこと)

POWER OF ATTORNEY: As a named inventor, I hereby appoint the following attorney(s) and/or agent(s) to prosecute this application and transact all business in the Patent and Trademark Office connected therewith: (*list name and registration number*)

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Japanese Language Declaration

(日本語宣言書)

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(Supply similar information and signature for third and subsequent joint inventors.)

Japanese Language Declaration
(日本語宣言書)

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第七の共同発明者の署名	日付	Seventh joint inventor's signature <i>Akira Ishida</i> Date Sept. 15, 2001
住所		Residence Oita, JAPAN SA
国籍		Citizenship Japanese
郵便の宛先		Post Office Address c/o KAWASUMI LABORATORIES, INC. 7-1, Oaza Tamada, Mie-cho, Ono-gun, Oita 879-7153

Japan

第四の共同発明者の氏名		Full name of fourth joint inventor, if any
第四の共同発明者の署名	日付	Fourth joint inventor's signature Date
住所		Residence
国籍		Citizenship
郵便の宛先		Post Office Address

第五の共同発明者の氏名		Full name of fifth joint inventor, if any
第五の共同発明者の署名	日付	Fifth joint inventor's signature Date
住所		Residence
国籍		Citizenship
郵便の宛先		Post Office Address

第六の共同発明者の氏名		Full name of sixth joint inventor, if any
第六の共同発明者の署名	日付	Sixth joint inventor's signature Date
住所		Residence
国籍		Citizenship
郵便の宛先		Post Office Address

(第六またはそれ以降の共同発明者に対しても同様な情報および署名を提供すること。)

(Supply similar information and signature for third and subsequent joint inventors.)